



PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

To: JANE MASSEY LICATA
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MARLTON, NJ 08053Docket System ☒
Status Report ☒
Docket Book ☒
NP = 12.25.01Date of Mailing
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23 MAR 2001

Applicant's or agent's file reference

RTSP-0057

IMPORTANT NOTIFICATION

International application No.

PCT/US00/16439

International filing date (day/month/year)

15 JUNE 2000

Priority Date (day/month/year)

25 JUNE 1998

Applicant

ISIS PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

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Authorized officer

KAREN A. LACOURCIERE

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RTSP-0057	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/16489	International filing date (day/month/year) 15 JUNE 2000	Priority date (day/month/year) 25 JUNE 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant ISIS PHARMACEUTICALS, INC.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 17 JANUARY 2001	Date of completion of this report 01 MARCH 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer KAREN A. LACOURCIERE
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/16489

I. Basis of the report**1. With regard to the elements of the international application:***☒ the international application as originally filed☒ the description:

pages 1-79 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the claims:

pages 80-81 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the drawings:

pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the sequence listing part of the description:

pages 1-15 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☒ contained in the international application in printed form.☒ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.**4. ☒ The amendments have resulted in the cancellation of:**☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig NONE**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).****

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 16-19 (in part)

because:

☒ the said international application, or the said claim Nos. 16-19 (in part) relate to the following subject matter which does not require international preliminary examination (*specify*).

Claims 16-19 are drawn to methods of treatment in a human, which is considered to be non-statutory, so the search was carried out and based on the alleged effects of the claimed compound/composition.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 16-19 (in part).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)

Claims	<u>1-19</u>	YES
Claims	<u>NONE</u>	NO

Inventive Step (IS)

Claims	<u>1-19</u>	YES
Claims	<u>NONE</u>	NO

Industrial Applicability (IA)

Claims	<u>1-19</u>	YES
Claims	<u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1-19 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest antisense targeted to ets-2 with a length of 8-30 nucleotides, and associated methods of inhibiting expression of ets-2.

Xian-Ming et al. teach a recombinant viral vector which expresses antisense to three genes, including c-ets-2 and teach inhibiting growth of human hepatome cells using said vector. Xian-ming et al., however, teach antisense molecules much larger than the 8-30 nucleobase molecules claimed and, further, do not teach antisense with the specific sequences and modifications claimed or making antisense to ets-2 in the size range claimed. Xian-Ming et al. do not teach any particular region of the ets-2 gene to target with antisense. The methods taught by Xian-ming et al. do not utilize ets-2 antisense alone, and it is unclear whether the antisense taught by Xian-ming et al. actually inhibit the expression of ets-2 and whether the ets-2 antisense is responsible for the inhibition of cell growth. The observed inhibition of cell growth may be due to inhibition of expression of one of the other genes targeted. Therefore, Xian-ming et al. does not teach or fairly suggest the antisense molecules or methods claimed.

Watson et al. teach the full length gene sequence of ets-2, however, Watson et al. do not teach or fairly suggest targeting ets-2 with antisense, nor do they teach or suggest antisense with the specific sequences claimed.

Milner et al. teach general methods of screening for antisense molecules to any gene, but do not teach or fairly suggest targeting the ets-2 gene with antisense, nor do they teach or fairly suggest antisense with the particular sequences claimed.

Baracchini et al. teach generally modifications to antisense, but do not teach or fairly suggest antisense targeted to ets-2, nor do they teach or fairly suggest antisense with the (Continued on Supplemental Sheet.)

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Suppl mental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): CO7H 21/04, 21/02; C12N 15/85, 15/86; A61K 35/00, 48/00; C12Q 1/68 and US Cl.: 436/ 6, 91.1, 91.3, 325, 375; 536/23.1, 23.2, 24.5, 24.3, 24.31, 24.33; 514/44

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
particular sequences claimed.

NEW CITATIONS

NONE